FDA's Role in Ensuring American Patients Have Access to Safe and Effective Medical Device Technology

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
U.S. FOOD AND DRUG ADMINISTRATION

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Executive Summary

Over the past five years, the Food and Drug Administration's device program has shown a pattern of markedly improved performance. Today it is performing strongly across a wide range of performance measures. At the same time, FDA has implemented a range of initiatives to promote access to safe and effective medical devices for American patients.

These improvements include those to 510(k) and premarket approval (PMA) review times along with a reduction in Investigational Device Exemption (IDE) review times of almost a full year—which means many devices investigated in the United States now reach the market a full year sooner than they did at the beginning of this decade. Performance in FDA's review of novel, moderate risk devices has also improved markedly, demonstrating the success of FDA's efforts to expand use of its *de novo* review pathway.

Importantly, these advances in the performance of the device program reflect a combination of programmatic improvements and innovative approaches to applying existing authorities, rather than changes to the basic framework for device oversight that was put in place almost 40 years ago. The existing framework assures that FDA's level of oversight matches the level of device risk, and applies flexible standards to premarket review of devices without compromising the standard for safety and effectiveness of devices. Enactment of the Food and Drug Administration Safety and Innovation Act (FDASIA) and increased Medical Device User Fee Act (MDUFA) funding facilitated some of the performance improvements in the device program. But neither FDASIA nor MDUFA altered the fundamental components of FDA's flexible, risk-based framework for device oversight.

Recent programmatic improvements and policy changes implemented by FDA, on its own initiative, include:

- Implementing a clinical trials program, dramatically improving its performance in reviewing clinical investigations of devices and building on the device program's longstanding interest in encouraging the use of innovative methodologies and study designs, such as the use of adaptive trial designs, where appropriate. This program has shown early success by encouraging companies to initiate early feasibility studies of devices in the United States, a development that can be expected to result in earlier access to those devices for American patients.

- Recalibrating the benefit-risk framework used in premarket review of devices and developing several new policies to include patient preferences in evaluating the risks and benefits of a device and speed access to devices with important benefits for American patients who have few options.

- Co-founding a public-private partnership and implementing new policies to promote the development and qualification of regulatory science tools and real world evidence for use in device development and assessment, as well as surveillance of the real world performance of medical devices.

- Adapting premarket and postmarket oversight to keep pace with rapidly evolving new technologies, including mobile medical apps and other health information technology (IT), companion diagnostics, and next generation sequencing tests.

This paper discusses these initiatives and shows how FDA's device program has adapted to changes in the marketplace, scientific advances, and new technology—all under the existing flexible, risk-based framework for oversight of medical devices. This framework continues to serve the American public well by promoting access to devices of public health importance, while protecting American patients from devices that are unsafe or ineffective.

Introduction

Advances in medical technology are transforming established medical practice and bringing completely new models of treatment, prevention, and diagnosis to patients right now. New devices include not only improvements over existing technology—devices that make less-invasive treatments possible and provide new options to patients whose conditions would have been considered untreatable in the past—but also technologies that will be keystones in emerging fields such as precision medicine. Genetic testing offers the promise of targeting the right treatment to the right patients, reducing ineffective treatment decisions and speeding the delivery of therapies that work. Health IT can empower people with chronic diseases to manage their own health and well-being by putting medical "apps" into the hands of patients. The FDA has responded to the promises and challenges posed by these devices with flexible risk-based approaches to its oversight role along with strong performance in bringing new, safe and effective products to market.

Glossary of Key Terms

510(k)	An application to FDA for market clearance of class II devices and a small number of class I devices. The manufacturer must demonstrate that the device is "substantially equivalent" to a legally marketed device. FDA currently reviews 510(k)s for fewer than 10 class III devices that were legally marketed before 1976. FDA is in the process of reclassifying or finalizing calls for PMAs for these devices.
De Novo	A premarket request for FDA to classify a novel device into class I or class II.
IDE	Investigational Device Exemption. An application to conduct studies of devices on human subjects.
MDUFA	Medical Device User Fee Act. An agreement between FDA and industry that FDA will take certain actions and meet performance goals in exchange for industry user fees.
PMA	Premarket Approval Application. The application to FDA for class III devices. The manufacturer must demonstrate a reasonable assurance of safety and effectiveness to gain approval for a PMA.

At the same time, FDA needs to ensure it is delivering on its oversight role. This role requires that FDA facilitate device innovation and patient access to new medical technology while providing the oversight to minimize unnecessary risks and ensure devices provide clinical benefit. At one end of the spectrum, unnecessary regulatory burden could drive innovators to seek more favorable environments, potentially depriving American patients of timely access to needed therapeutic and diagnostic devices.

At the other end of the spectrum, lax oversight could lead to patient harm from devices that have not been tested and shown to be safe and effective. Lax oversight also could affect the marketplace by reducing confidence in the healthcare system that devices will do what they are intended to do without harming the patients they are intended to benefit. A flexible, risk-based approach to oversight of medical technology is critical to striking the right balance.

FDA's existing framework establishes flexibility that has allowed the agency to develop innovative approaches to medical device oversight. These approaches reduce unnecessary burden without compromising assurances that devices marketed to American patients are safe and effective. Improvements to FDA's device program have already resulted in decreased review times and patient access to important new devices. And while other changes are too new to evaluate, early signs are positive and point to additional improvements in timely access for American patients to safe and effective devices.

The U.S. Regulatory Environment for Devices: 2010–2015

Performance of FDA's Device Program

In the early part of this decade, many policymakers and FDA stakeholders called for reform of FDA's device program, arguing that FDA regulation was driving companies to relocate overseas or market their devices abroad before introducing them in the United States. To support their arguments, critics pointed to contemporary surveys of device manufacturers. Although FDA raised questions about the methodology used in some of these studies,[1] the underlying premise that industry's perception of FDA oversight can affect decisions about introducing new technology in the US marketplace is important.

Moreover, in 2010, FDA conducted its own assessment, including data analyses. It found a steady decline in the performance of its premarket program from as early as 2000 for some indicators continuing to 2010. FDA also identified underlying root causes. In response, the agency implemented a number of new policies and programmatic changes over the past five years to improve its performance and to adapt its oversight to the global marketplace and to new technologies. Added funding and

[1] These arguments often rely on studies published early in this decade to support these assertions, studies the methodology of which FDA has questioned. See Letter from Jeanne Ireland, Assistant Commissioner for Legislation, FDA, to Ranking Member Henry A. Waxman (July 11, 2011) http://democrats.energycommerce.house.gov/sites/default/files/documents/Waxman-FDA-Concerns-Regarding-Makower-Study-of-Medical-Device-Regulation-2011-7-18.pdf

increased capacity, as the result of the 2012 reauthorization of MDUFA, also helped reverse the direction of the agency's medical device premarket program.[2]

Today, the performance of FDA's device program has significantly improved. FDA is on track to meet all of its MDUFA performance goals related to device review. Premarket performance measures of FDA's device program show marked improvement since the start of the current decade on several measures related to how quickly devices come to market in the United States.

FDA is making progress in reducing total review times for 510(k) submissions, de novo requests, IDEs, and the higher-risk PMA applications. While data is not complete for the years 2013 and 2014 because some applications remain open, existing data show improvements on several important measures:[3]

- Time to decision on device submissions has decreased:
    - **510(k)s**: The vast percentage of device premarket submissions received by FDA in any given year are 510(k)s. In fiscal year (FY) 2010, it took 132 days for a total time to decision on a 510(k). By FY 2014, total time had dropped by 13 percent to about 115 days. (These figures compare review times when 88.3 percent of submissions are closed.) Organizationally, the medical device premarket review offices at FDA's Center for Devices and Radiological Health (CDRH) are divided into review divisions, which are composed of review branches. FDA is also closing the gap between the branches with the fastest and slowest review times. In 2003, the lowest performing branch reached 34 percent of its 510(k) MDUFA decisions within 90 FDA Days (the time spent by FDA reviewing the application). In 2014, most branches were reaching decisions within 90 FDA days 90 percent of the time or better, with the lowest performing branch reaching 81 percent of its 510(k) MDUFA decisions within 90 FDA Days.
    - **PMAs**: Original PMAs generally account for only about 1 percent of all device applications received by FDA. Average total time to decision in FY 2014 has decreased to 242 days from 352 days at its peak in FY 2009, for an improvement of 31 percent. (These figures compare review times when 64 percent of applications are closed.) Once all FY 2014 applications are closed, we project performance will meet or exceed FY 2012 levels, which would be at least a 36 percent improvement since 2009. FDA is also closing the gap between the divisions with the fastest and slowest review times. Performance

[2] FDA estimates that it has added at least 190 of the planned 240 staff authorized by MDUFA III since the end of FY 2011. These additional staff members have contributed to FDA achieving the new performance goals under MDUFA III.

[3] **Appendix A** provides additional data showing the current performance of FDA's device program, including data that show the course of improvement over the past five years.

has improved significantly, from a difference in total average days to final decision between the highest and lowest performing divisions of 633 days in FY 2008 to 197 days in FY 2014.

  - **IDEs:** Median total time to full IDE approval decision has decreased by over a year, from 442 days in FY 2011 to 30 days in FY 2015. The percent of IDEs approved within two cycles increased from 15 percent in FY 2011 to 63 percent in FY 2014 and 72 percent in FY 2015.
  - ***De novo:*** The average total time to final decision for de novo requests (510(k) plus *de novo* review) submitted after a device was found to be not substantially equivalent through the 510(k) process has been reduced from 992 days in FY 2010 to 300 days in FY 2014.

- Another measure of the performance of the medical device program is that FDA is working with industry to ensure that submissions are complete and ready for review. As a result, the percentage of submissions that are cleared and approved has increased since 2010:
  - The percentage of 510(k)s cleared increased from 73 percent in FY 2010 to 84 percent in FY 2014.
  - The percentage of PMAs approved increased from 59 percent in FY 2010 to 86 percent in FY 2014.
- The number of pending submissions at the end of a year has significantly decreased since 2010:
  - The number of 510(k) submissions pending has been reduced by 30 percent.
  - The number of PMA submissions pending has been reduced by 43 percent.

In 2014, FDA's Center for Devices and Radiological Health made providing excellent customer service a strategic priority. So it launched an effort to improve customer service that included staff training; surveys to assess customer interactions and measure customer satisfaction; and, based on feedback from customers, actions to improve the quality of activities and services. Understanding and proactively addressing, as appropriate, the needs of all of FDA customers—including patients, practitioners, industry, and agency staff—can improve the timeliness, quality, and consistency of the agency's decision-making and customer satisfaction. High levels of customer satisfaction can help make the United States a more attractive marketplace for early patient access to safe and effective devices of public health importance. As this FDA center has made improvements to its program, customer satisfaction has improved. In fact, its 2015 survey results show an overall 88 percent customer satisfaction rating, with the rating for the premarket program even higher at 93 percent.

Framework for Device Oversight

The basic framework under which FDA oversees devices was put in place almost 40 years ago, when Congress enacted the Medical Device Amendments of 1976 (MDA). The MDA established a flexible framework for FDA's oversight of medical devices and required that FDA tailor its oversight of devices to the degree of risk presented. Although the framework established under the MDA recognizes that medical devices inherently carry risk, the MDA did not mandate that FDA eliminate risk. Rather, FDA applies only the level of oversight necessary to establish a reasonable assurance of safety and effectiveness for devices. Under this framework, only about half of all devices are subject to any premarket review by FDA. And for the devices that are subject to premarket review, FDA reviews clinical data for fewer than 20 percent of these products because there are other, less burdensome means to determine that there is a reasonable assurance that a device is safe and effective.[4]

FDA oversight of devices is tailored to three risk-based classifications:

- **Class I, or low-risk devices**: FDA does not review any premarket information for class I devices, with the exception of a small subset of class I "reserved" devices. Class I makes up about 50 percent of all medical devices. Examples of class I devices are medical device data systems (health IT used only to exchange, store, retrieve, display, or change the format of electronic data).
- **Class II, or moderate-risk devices**: FDA generally reviews 510(k) submissions for these devices, which requires a demonstration of substantial equivalence to a legally marketed device. About 80 percent of all 510(k)s contain only non-clinical data. Examples of class II devices include glucose test strips and infusion pumps.
- **Class III, or high-risk devices**: FDA generally reviews PMAs containing clinical and non-clinical data to determine whether there is a reasonable assurance of safety and effectiveness for these devices. FDA generally reviews around 40 PMAs a year. Examples of PMA devices include heart valve replacements and diagnostic tests used to select ovarian cancer patients for a drug regimen.

FDA's evidentiary standard for premarket review of devices is valid scientific evidence, a standard established by Congress in 1976 that still sets the benchmark for evidence to support premarket

[4] The 20 percent includes *in vitro* diagnostics (IVD) devices which typically contain test results based on human-derived samples. When IVDs are excluded, the number of submissions with clinical data drops to fewer than 10 percent.

submissions. This benchmark assures that the evidence is of sufficient quality that it can be relied on to determine whether or not a device should be approved or cleared. Although valid scientific evidence includes randomized controlled clinical trials, the overwhelming majority of devices come to market based on non-clinical data, small clinical studies, or both. The valid scientific evidence standard encompasses many other forms of evidence, such as bench testing, journal articles, observational data, and foreign studies.

In vitro diagnostic (IVD) devices have been regulated by FDA under its risk-based device framework since the inception of the device program. Diagnostic tests can be used in the context of acute outbreaks, such as the recent Ebola outbreak, and in the diagnosis and treatment (including management) of chronic diseases such as cancer and diabetes. Success in combating these diseases depends on diagnostic tests that can accurately detect them and be used to select and manage treatments. One example is the widespread use of glucose meters and diabetes test strips. These devices can empower people with diabetes to manage their disease independently, but only when the devices are accurate. In recent years, test reports of falsely high and low blood sugar levels have led to multiple recalls of these products over concerns that false readings could lead to incorrect treatment decisions. In particular, insulin administered in response to falsely high measures of blood sugar could lead to acute hypoglycemia, coma, and even death if left untreated. The American Diabetes Association has issued a statement of strong support of FDA oversight of these tests, stating:

> The American Diabetes Association strongly endorses [FDA] oversight of test strip manufacturers[…]. The Association applauds the FDA's requirements that all test strips meet existing FDA standards for medical devices, since those standards are designed specifically to require the greatest accuracy in readings when an error would place a patient's health and life in danger. [5]

For *in vitro* diagnostic devices, a reasonable assurance of safety and effectiveness means that a test has analytical and clinical validity. Analytical validity assesses how well the test detects or measures certain markers in human specimens. Clinical validity assesses whether the marker has clinical significance, such as correlation with disease or the ability to predict a therapeutic response to a drug. As FDA's recent announcement that it intends to exempt carrier screening tests from premarket review shows, the level of data FDA requires to demonstrate analytical and clinical validity for *in vitro* diagnostic devices depends largely on risks from the device.

The central features of FDA's device program—a risk-based framework that tailors oversight to device risk; a flexible review standard that requires a reasonable assurance of safety and effectiveness; and an

[5] http://professional.diabetes.org/News_Display.aspx?CID=93129

adaptive but scientifically grounded evidentiary standard of valid scientific evidence—have served the public well. While there have been multiple amendments to FDA's original authority, providing new premarket pathways and enhancing FDA's post-market oversight, the framework put in place by the MDA continues to provide the tools to assure safety and effectiveness of therapeutic and diagnostic devices while allowing FDA to adapt its oversight to the demands of rapidly evolving medical technology.

Adapting FDA's Oversight Role to Current Challenges: 2010–2015

The new policies and programmatic changes FDA has implemented in the past five years respond to the needs of American patients to have timely access to high-quality, safe, and effective devices, and to challenges created by rapidly evolving fields of medical innovation. These initiatives have had far-ranging objectives, from providing FDA review staff with new tools to assess the benefits and the risks of a device to American patients, to promoting regulatory certainty and empowering patients to manage their well-being. Among these initiatives are process improvements and policy changes to the agency's oversight of clinical investigations of devices.

Streamlining Clinical Trials

In 2014, FDA established a Clinical Trials Program to coordinate its oversight of clinical studies of devices, provide interventions if a review of an application to conduct a clinical investigation of a device (Investigational Device Exemption) takes more than one cycle, offer more opportunities for interactions with sponsors, expand training for review staff, and establish new or modified policies in this area. For example, recognizing that devices that are studied in the United States in the early stages of clinical assessment are more likely to reach American patients sooner in pivotal trials and as marketed devices, FDA implemented a pilot program in 2011 to encourage early feasibility studies, or early stage clinical studies, of devices in the United States. In 2013, FDA issued final guidance on early feasibility studies;[6] under this program, FDA may accept a higher degree of uncertainty during the device development process to facilitate important early clinical evaluation of promising technologies.

[6] *Investigational Device Exemptions (IDEs) for Early Feasibility Medical Device Clinical Studies, Including Certain First in Human (FIH) Studies: Guidance for Industry and FDA Staff* (October 1, 2013), available at http://www.fda.gov/downloads/medicaldevices/deviceregulationand%20guidance/guidancedocuments/ucm279103.pdf.

As a result, the agency is beginning to see an increase in companies submitting IDEs for early feasibility studies in the United States and more approvals of such IDEs. In the past two years FDA has reduced the median time to approval for early feasibility studies by nearly 70 percent: from 226 days in FY 2013 to 66 days in FY 2015.

Devices studied in the United States in the early stages of development are more likely to reach American patients sooner in pivotal studies and as marketed devices. In the past 15 fiscal years, for those original PMAs whose approval was based on FDA approved pivotal clinical studies, 94 percent (283 out of 300) of these approvals were based on a single pivotal clinical study. More recently, in the past five years, the number has increased to 98 percent (82 out of 84). Of the 82 FDA approved original PMAs whose approval was supported by a single pivotal clinical study, 32 (39 percent) included studies enrolling subjects outside the United States. For *in vitro* diagnostic devices, where clinical studies are typically conducted in at least three sites, sponsors generally choose to have one of those sites inside the United States to address differences between the United States and other countries in how medicine is practiced, patient populations, and disease progression.

FDA is facilitating and encouraging the use of innovative clinical trial designs and statistical methods such as adaptive clinical trials and Bayesian statistics. By incorporating existing clinical information about devices into statistical analyses, adaptive clinical trials such as the Bayesian approach can support a marketing application for a device based on shorter and smaller clinical trials. In 2010, FDA issued a guidance document on how Bayesian methods can be used to design and analyze data from medical device clinical trials.[7] In 2015, FDA issued draft guidance on how to plan and implement adaptive designs for clinical studies when used in medical device development programs.[8] FDA's efforts to promote the appropriate use of adaptive trial designs to support premarket device applications date to the late 1990s.[9] In recent years, many devices have come to market based on adaptive trial designs. For the period from 2007 to May 2013, FDA received 250 submissions that were adaptive, most of which were pre-submissions and IDEs. About 30 percent of these used Bayesian methods. In addition, there were 17 PMAs and PMA Supplements that used adaptive clinical trials from 2007 to May 2013, eight of which used Bayesian methodologies.

These programmatic improvements and policy changes have already yielded results in significantly reduced time to approval of IDEs and increasing approval rates. The full effect of these programmatic

[7] http://www.fda.gov/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm071072.htm

[8] http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/Ucm446729.pdf

[9] Gregory Campbell (2011) Bayesian Statistics in Medical Devices: Innovation Sparked by the FDA, *Journal of Biopharmaceutical Statistics*, 21:5, 871-887, DOI: 10.1080/10543406.2011.589638. This article refers to 16 approved PMAs that relied on Bayesian analysis and one cleared 510(k); there have been several additional device approvals since 2011 but an exact number is not available.

improvements on U.S. healthcare will not be known for several years. But streamlined processes for initiating device studies in the United States and reductions in the time to approval for U.S. clinical studies are promising developments in the effort to ensure American patients have timely access to medical devices of public health importance.

Flexible Decision-making

In recent years, FDA has also implemented a series of new premarket policies that build on the risk-based framework established by the MDA. While these policies are relatively new, and the programmatic effects cannot yet be measured, many of the policies have affected important review decisions, impacting public health by speeding access to new safe and effective devices.

Benefit-Risk: FDA's standard for premarket review of high-risk devices has always required FDA to weigh the benefits of a device against its risks. For the past three years, however, FDA has used a more flexible, patient-centric, and transparent benefit-risk framework to evaluate devices. Under this framework, developed with public feedback, reviewers weigh a number of factors to arrive at a decision of whether the benefits of a device outweigh its risks. These factors include the type, magnitude, and duration of a risk or benefit; the probability that a patient will experience the risk; patient tolerance for risk; availability of alternative treatments; and the value the patient places on treatment. Under this approach, devices that present a small but real likelihood of preventing serious disability or death could, with appropriate risk mitigation such as labeling, reach the market despite greater uncertainty about its risks. Also, in appropriate cases, FDA may defer some data that would be otherwise collected premarket to the postmarket setting. It would do so to promote timely access to the benefits of devices of public health importance, provided there is still a reasonable assurance of safety and effectiveness. FDA currently applies this benefit-risk framework to all reviews of high-risk and novel lower risk devices.[10]

Patient Preferences Initiative: Increasingly, patients seek to be involved in decision-making about their own health. Recognizing the importance of considering patients' views in deciding how the probable risks and benefits of medical technology should be weighed, in 2013 FDA launched the Patient Preferences Initiative. The initiative seeks to incorporate valid scientific evidence of patient preferences on the benefit-risk tradeoffs of medical devices into premarket review and other decision-making by FDA's device program. For example, a team of FDA scientists published an article with

[10] http://www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm296379.pdf.

leading behavioral economists to illustrate how patient preferences can inform medical device approval decisions.[11] The authors successfully tested a new method for capturing patient sentiment and translated it into a decision-making tool for incorporating patient preferences into clinical trial design for obesity treatments. They were able to estimate the tradeoffs in risks that obese patients are willing to accept in exchange for a certain amount of weight loss, and the minimum number of pounds patients would have to lose to tolerate the risks of a weight loss device. FDA used the results of this study to inform the approval decision for a new weight loss device: the Maestro Rechargeable System, the first FDA-approved obesity device since 2007. In 2015, FDA issued a draft guidance addressing how patient preference information can be collected and used in decision making relating to PMAs, Humanitarian Device Exemption (HDE) applications, and *de novo* requests. The draft guidance also outlines considerations for including patient preference information in labeling for patients and health care practitioners.[12]

Expedited Access Pathway Program: In 2014, FDA proposed a program for expedited patient access to devices that are of potential significant public health benefit because they are intended to treat or diagnose patients with life-threatening or irreversibly debilitating conditions whose medical needs are unmet by current technology. (Some also have called these products "breakthrough devices.") Under this pathway program, FDA would provide earlier and more interactive engagement with sponsors of such devices. This engagement includes the involvement of senior management and the development of a collaborative plan for collecting the scientific and clinical data to support approval—features that, taken together, should provide patients with earlier access to safe and effective medical devices. The program would target devices with potentially high impact on patient health because, for example, they fulfill an unmet need by offering an important advantage over existing devices. To promote earlier patient access, some data collection for devices marketed under this pathway might be moved from premarket to postmarket, provided there is still a reasonable assurance of safety and effectiveness concerning the device. FDA issued final guidance[13] in April 2015. The Expedited Access Pathway Program went into effect on April 15, 2015.

[11] Marin P. Ho et al., Incorporating Patient-Preference Evidence into Regulatory Decision-Making, *Surgical Endoscopy* DOI 10.1007/s00464-014-4044-2 (2015).

[12] http://www.fda.gov/ucm/groups/fdagov-public/@fdagov-meddev-gen/documents/document/ucm446680.pdf

[13] http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM393978.pdf

Regulatory Science: New Uses of Evidentiary and Analytical Tools

FDA also has invested in several new regulatory science programs over the past several years to reduce the time and cost, but not quality, of data development for devices. These programs promote the development and use of tools, analytical methods, and data sources in premarket applications to bring safe and effective devices to market faster and at less cost.

Medical Device Development Tools (MDDTs): An MDDT is a scientifically validated tool—a clinical outcome assessment (e.g., patient-reported or clinician-reported rating scales), a test used to detect or measure a biomarker, or a non-clinical assessment method or model (e.g., an *in vitro*, animal or computational model)—that aids device development and regulatory evaluation. In August 2014, FDA announced a pilot program under which anyone can submit scientific information to FDA to qualify an MDDT. Once qualified, MDDTs can be used to support premarket applications.[14] In practice, this can enable sponsors to support a PMA, *de novo* request, or a 510(k) using smaller and shorter clinical trials. The MDDT program builds on FDA's success in developing computational models like the Virtual Family (VF), a set of highly detailed, anatomically correct, computational whole-body models, designed to mimic humans of both sexes at various stages of growth.[15]

Medical Device Innovation Consortium: In 2012, FDA and LifeScience Alley (a biomedical trade association) co-founded a new nonprofit partnership: the Medical Device Innovation Consortium (MDIC). This was the first public-private partnership (PPP) with a mission to advance medical device regulatory science. MDIC is a collaboration among federal agencies, industry, nonprofit organizations, and patient advocacy organizations. It provides a venue for leveraging resources, people, and intellectual capital to find solutions to common challenges in the precompetitive space. MDIC supports the development of non-clinical device development tools that can reduce the need for or size of clinical studies to support market approval as well as steps to reduce the time and cost of clinical trials. MDIC has several active project focus areas, including the following:

> *Patient Centered Benefit-Risk*: This project focuses on developing scientifically robust ways to measure patient perspectives on the benefits and risks of medical devices, and a framework for incorporating patient perspectives into device development and regulatory decision-making. In May 2015, MDIC released a framework for integrating patient perspective into medical device

[14] *See* 79 *Federal Register* 48170. FDA has also issued draft guidance on the qualification process for MDDTs. *See Medical Device Development Tools, Draft Guidance for Industry, Tool Developers, and Food and Drug Administration Staff* (November 13, 2013), available at http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM374432.pdf

[15] http://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDRH/CDRHOffices/ucm302074.htm

benefit-risk assessments and other parts of the total product lifecycle.[16] The framework includes an appendix of tools that could be used to gather patient preference information.

Clinical Trials Innovation and Reform: MDIC is working with FDA, the National Institutes of Health, industry, academia, and patient groups to explore ways to improve the efficiency and cost-effectiveness of medical device clinical trials while maintaining data quality. The goal is to streamline the clinical trial process and restore the United States to the country of first choice to conduct clinical research for medical technology innovation. The project seeks to innovate and reform the U.S. clinical trial process by defining and tackling top barriers to efficient design and conduct of medical device clinical trials.

Computer Modeling and Simulation: The project's goal is to reduce the time and cost of bringing devices to market while improving patient safety by advancing the science around computer modeling and simulation for medical devices. These models, when of sufficient quality to be considered "regulatory grade," can be used to assess device performance. Thus, they can reduce or obviate the need for other more expensive or burdensome types of scientific evidence (such as human clinical studies).

MDIC's collaborations focus on advancing regulatory science to propel device development through the regulatory process and to market, resulting in smarter regulation and earlier patient access to safe, effective, and high-quality devices.

Regulatory Science: The Virtual Family

FDA collaborated with researchers and industry to create the Virtual Family, a set of four highly detailed, anatomically correct whole-body models of an adult male, an adult female, and two children. Currently, the VF models are used for electromagnetic, thermal, acoustic, and computational fluid dynamics (CFD) simulations. These simulations can supplement or replace data from clinical investigations of devices. As of the end of 2014, the VF was used in more than 120 medical device submissions to FDA and was cited more than 180 times in peer-reviewed literature. Recently the Virtual Family 3.0 became available; it is available free of charge to researchers for use in device development.

[16] "A Framework for Incorporating Information on Patient Preferences Regarding Benefit and Risk into Regulatory Assessments of New Medical Technology," available at http://mdic.org/framework-report/

Real World Data: In September 2012, the FDA published a report, *Strengthening Our National System for Medical Device Postmarket Surveillance,* which proposed a National Medical Device Surveillance System (MDS) for improving and addressing the limitations of the agency's current system for monitoring medical device safety and effectiveness. This report recommended establishing a national infrastructure for gathering and analyzing real world data, or data collected as part of routine clinical practice and patient experience. The purpose of such a national system is to identify potential safety signals in near real-time; better understand the benefit-risk profiles of medical devices on the market; and facilitate the clearance and approval of new devices, or new uses of existing devices.

In the past year, FDA has achieved tremendous progress laying the groundwork for the MDS. FDA has begun implementing the unique device identification (UDI) rule for the highest-risk devices, including development of a Global UDI Database (GUDID) as the repository for information that unambiguously identifies devices through their distribution and use. By promoting incorporation of UDIs into electronic health information (such as electronic health records, also called EHRs, and device registries), a vast quantity of untapped real world data from clinical experience with devices housed in EHRs and other electronic information sources may become available for use in understanding the benefit-risk profiles of medical devices. In addition, FDA continues to build registry capabilities both domestically (such as the National Breast Implant Registry) and internationally (such as the International Consortium of Vascular Registries). FDA established a Medical Device Registry Task Force consisting of key registry stakeholders as part of the Medical Device Epidemiology Network (MDEpiNet) Program, a collaborative program that FDA co-founded to develop new and more efficient methods to study medical devices and to enhance FDA's ability to more fully understand the safety and effectiveness of medical devices after they are marketed. The Task Force will issue its recommendations during summer 2015. FDA commissioned the Engelberg Center for Health Care Reform at the Brookings Institution to convene and oversee deliberations of the Medical Device Postmarket Surveillance System Planning Board. In February 2015, the Medical Device Postmarket Surveillance System Planning Board issued a report, *Strengthening Patient Care: Building an Effective National Medical Device Surveillance System,* outlining recommended steps toward the development, oversight, and effective use of medical devices, while supporting improvements in patient safety and health outcomes.

FDA's work in developing registries has relieved postmarket burden by allowing device sponsors to submit data from registries instead of conducting their own new postmarket studies. FDA is also pursuing strategies to use data from the most robust registries in the premarket context and has already relied on registry data to expand access to transcatheter aortic valve replacement devices.

Use of Real World Evidence to Expand Use of Minimally Invasive Heart Valve Replacement

In 2011, transcatheter aortic valve replacement (TAVR), a minimally invasive alternative to open-heart surgery, was indicated only for patients with aortic stenosis for whom open heart surgery was too risky, and who were not yet healthy enough to undergo certain placement procedures. The agency expanded approval for the device, the Edwards SAPIEN, less than a year later. But TAVR was still indicated only for insertion through the artery in the leg or via the apex of the heart (the lowest tip), excluding a significant number of patients who were poor candidates for these procedures.

Clinical experience indicated this device also could offer good outcomes to inoperable patients who needed other access sites. In 2013, FDA approved revisions to the device labeling to also cover inoperable and high-risk patients who need their devices inserted through alternative access points. Data collected from a related patient registry played a key role in this decision, as the FDA approved the labeling change based in large part on available registry data.

Adapting to New Technology

FDA's device program can and has adapted to new technologies. For example, recent policies have focused FDA oversight of health IT on medical devices that present greater risks, with the goal of permitting access to a range of products while ensuring the safety and effectiveness of a subset of mobile medical apps that present greater risk to patients if they do not work as intended—such as those used to treat or diagnose patients. FDA's device program is leading the development of clear, streamlined pathways for technologies that are pivotal to the success of precision medicine, such as companion diagnostics and Next Generation Sequencing tests. The approach to oversight in these areas demonstrates the adaptability of the existing regulatory framework and the responsiveness of FDA's device program to challenges presented by new technology.

Mobile Medical Applications and Other Health IT: As the number and functionality of mobile applications (apps) exploded in recent years, FDA saw the need to clearly articulate a policy to provide clarity and certainty for medical app developers, as well as to the healthcare practitioners and patients who use them. In 2013, FDA announced a policy under which it intended to focus its regulatory oversight on those mobile apps[17] that are medical devices and pose the greatest risk to consumers and to exercise enforcement discretion for the majority of mobile apps that are medical devices, as they pose minimal risk to consumers. FDA followed this policy with a preliminary health IT report produced in collaboration with the Office of the National Coordinator and the Federal Communications

[17] *Mobile Medical Applications: Guidance for Industry and Food and Drug Administration Staff* (February 9, 2015), available at http://www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm263366.pdf.

Commission, as required by FDASIA in 2012.[18] This report outlines a series of recommendations and actions for the public and private sectors to take for health IT that is not actively regulated by FDA or subject to FDA's jurisdiction. These activities are intended to avoid duplicative regulation while promoting innovation and protecting patient safety. The agencies accepted public comment on this report to inform its development. Recently, FDA has issued guidance under which it clarified that it intends to exercise enforcement discretion for medical device data systems,[19] a form of health IT that, while low risk, is widely used in the delivery of health care. With these actions, FDA helped to make clear the narrow arena of health IT where the agency intends to continue its oversight—namely, the space occupied by the riskiest forms of medical device software—while clearly stating its intention to not focus oversight over a broad range of other medical device software products.

FDA recently proposed a similar policy for all low-risk devices used to promote health and well-being and help individuals with chronic disease maintain wellness. The policy extends to products used to promote physical fitness, maintenance of a healthy weight, relaxation, and similar states of well-being, so long as the product does not present inherent risks to users. As with FDA's recent policies concerning health IT, FDA proposed this policy to provide greater certainty to product developers and users that FDA intends to focus its oversight in these emerging areas of product development on medical devices that present more than a low risk.

Companion Diagnostics: Companion diagnostic tests play an important role in promptly determining which therapies are safe and effective for a particular patient. They are a key component of precision medicine. FDA has approved 20 companion diagnostic tests, all of them within the Prescription Drug User Fee Act (PDUFA) performance goals for the corresponding drug or biological product, ensuring the timely marketing authorization of both. In 2014, FDA issued guidance[20] describing a clear marketing pathway for developers of companion diagnostic tests and pharmaceutical manufacturers, receiving strong support from both pharmaceutical and conventional test manufacturers for providing regulatory clarity in this rapidly advancing area of medicine. Companion diagnostics that FDA has approved in recent years include the BRACAnalysis CDx™ test, a laboratory developed test that aids in determining which ovarian cancer patients are more likely to respond to the drug Lynparza™ (olaparib) based on certain BRCA variants; the THxID™ BRAF Kit, which detects certain mutations in melanoma tissue samples to aid in selecting patients for drug therapy with Tafinlar® (dabrafenib) or Mekinist™

[18] See FDASIA Health IT Report (April 2014), available at http://www.fda.gov/downloads/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDRH/CDRHReports/UCM391521.pdf

[19] *Medical Device Data Systems, Medical Image Storage Devices, and Medical Image Communications Devices: Guidance for Industry and Food and Drug Administration Staff* (February 9, 2015), available at http://www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm401996.pdf

[20] *In Vitro Companion Diagnostic Devices: Guidance for Industry and Food and Drug Administration Staff* (August 6, 2014), available at http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM262327.pdf.

(trametinib); and the *therascreen®* KRAS RGQ PCR Kit, a test that screens out colorectal cancer patients with genetic mutations known to predict a nontherapeutic response to the biological products Erbitux® (cetuximab) and Vectibix® (panitumumab).

Next Generation Sequencing: Cystic Fibrosis

FDA authorized marketing for the Illumina MiSeqDx Cystic Fibrosis System *in vitro* diagnostic test, which detects 139 genetic mutations that are relevant to whether an individual will develop cystic fibrosis or transmit the cystic fibrosis genetic mutation to his or her children. FDA worked with the test developer to apply novel approaches to establishing clinical validity by using publically available quality-weighted human reference genome (databases) that was created through collaboration between the FDA and the National Institutes of Standards and Technology (NIST) and analytical validity by using data showing the test could accurately detect a representative sample of variants.

Next Generation Sequencing: Many newly developed genomic diagnostic tests rely on next generation sequencing (NGS), an advanced technology, which is becoming a keystone of precision medicine. NGS tests can rapidly generate an unprecedented amount of genetic data for each patient. Most *in vitro* diagnostic devices are used to detect a single or a defined number of markers to diagnose a limited set of conditions; in contrast, a single NGS test can identify thousands or millions of genetic variants that can be used to diagnose or predict the likelihood of an individual developing a variety of diseases. FDA has provided marketing authorization for an NGS test for cystic fibrosis using innovative approaches to establishing the test's effectiveness. As part of President Obama's Precision Medicine Initiative, FDA will develop a new approach for evaluating NGS technologies to facilitate the generation of knowledge about which genetic changes are important to patient care and foster innovation in genetic sequencing technology, while ensuring that the tests are accurate and reliable.

FDA recently published a white paper outlining a possible approach to review of this technology that would greatly reduce burden by leveraging data in existing high-quality, curated genetic databases as an alternative to conducting new clinical trials and by reviewing analytical performance for only a subset of variants through the creation and use of reference standards. FDA has received positive feedback from thought leaders in this area for identifying ways to adapt its review practices to this important new technology.[21]

[21] Lander, Eric S., Cutting the Gordian Helix—Regulating Genomic Testing in the Era of Precision Medicine, *NEJM* 2015, DOI: 10.1056 p150.

Conclusion

This is a time of remarkable advances in medical device technology, which can extend lives and minimize suffering for American patients. New technologies hold promise for empowering patients in their own healthcare decision-making and for delivering precision treatments that are truly targeted to individuals. But the promise of advances in medical technology will only be realized if the patients and providers who use them are confident that they are safe and can do what they are intended to do.

FDA's device program has evolved alongside changes in medical technology and in the global marketplace. The agency has implemented several new policies and programmatic improvements to ensure American patients have timely access to devices without compromising standards of safety and effectiveness. FDA has made its review of investigational devices more efficient and expeditious, streamlining the pathway to conducting clinical investigations in the United States. In addition, more devices that go through FDA's premarket program are being approved and cleared for marketing, and devices are coming to market more quickly.

Improvements in FDA's device program have occurred under a longstanding framework that tailors FDA oversight to a device's risks and benefits. This framework provides flexibility to adapt to new technology and to consider different forms of evidence. At the same time, the framework establishes a standard for devices marketed to American patients: There must be a reasonable assurance of safety and effectiveness for devices, demonstrated by valid scientific evidence. This framework serves the public well and allows the agency to meet the demands of rapid innovation and a changing global marketplace while promoting public confidence in high-quality, safe, and effective devices.

Appendix A. Medical Device Premarket Program Performance

MDUFA III

Performance Goals: Preliminary FY 2014 data for MDUFA performance goals through March 31, 2015, indicate that CDRH is on track to meet nearly all its performance goals while maintaining a high workload. In FY 2014, CDRH received more than 6,000 submissions for PMAs, PMA supplements, 510(k)s, *de novos*, and HDEs. The 2nd quarter MDUFA III Performance Report presents preliminary performance for the FY 2013, FY 2014, and FY 2015 MDUFA III submissions.[22] Further details can be found in the MDUFA III Quarterly Performance Reports available on FDA's MDUFA III website.[23]

Table 1. FY 2014 MDUFA III performance for selected submission types, as of March 31, 2015.

	Performance Goal	Current Performance[24]	Review Progress[25] (% complete)
Substantive Interaction	**75%**	**95%**	41 of 41 (100%)
Decision without Advisory Committee input	**80%**	**100%**	28 of 37 (76%)
Decision with Advisory Committee input	**70%**	**100%**	2 of 4 (50%)
180-Day PMA Supplements			
Substantive Interaction	**75%**	**95%**	177 of 177 (100%)
Decision	**90%**	**100%**	151 of 176 (86%)
Decision	**90%**	**99%**	331 of 331 (100%)
510(k) Premarket Notifications			
Substantive Interaction	**75%**	**97%**	3,465 of 3,483 (99%)
Decision	**93%**	**99%**	2,873 of 3,248 (88%)
CLIA Waivers			
Substantive Interaction	**95%**	**100%**	14 of 14 (100%)
Decision for dual submissions (510[k] and CLIA waiver)	**90%**	**100%**	1 of 1 (100%)
Decision without Advisory Committee input	**95%**	**100%**	13 of 14 (93%)
Decision with Advisory Committee input	**95%**	**-**	0 of 0

[22] http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/Overview/MedicalDeviceUserFeeandModernizationActMDUFMA/UCM446492.pdf

[23] http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/Overview/MedicalDeviceUserFeeandModernizationActMDUFMA/ucm109210.htm

[24] **Current** Performance presents the percentage of actions that FDA completed within the review-time goal as of March 31, 2015.

[25] **Review Progress** presents the number of FY 2014 submissions that had actions taken as of March 31, 2015, plus submissions pending but overdue as of March 31, 2015 out of all MDUFA cohort submissions.

Premarket Notification (510[k]) Program

Average Time to Decision for 510(k)s: Total time to decision includes the time spent by FDA reviewing the application (FDA Days) as well as the time spent by the submitter responding to questions from FDA (Submitter Days). 510(k) average total time to decision has decreased since its peak in FY 2010 (**Chart 1**)**.** The FY 2014 cohort is not yet fully closed; as of March 31, 2015, the 2014 cohort was 88.3 percent closed. Comparison of receipts cohorts at the same closure[26] levels show a 17 percent decrease in total review time (**Chart 1**) between FY 2010 and FY 2013 and a 13 percent decrease in total review time between FY 2010 and FY 2014 (**Chart 2**). The FY 2013 cohort had similar average total time to decision when compared with FY 2014 at the 88.3 percent level of closure.

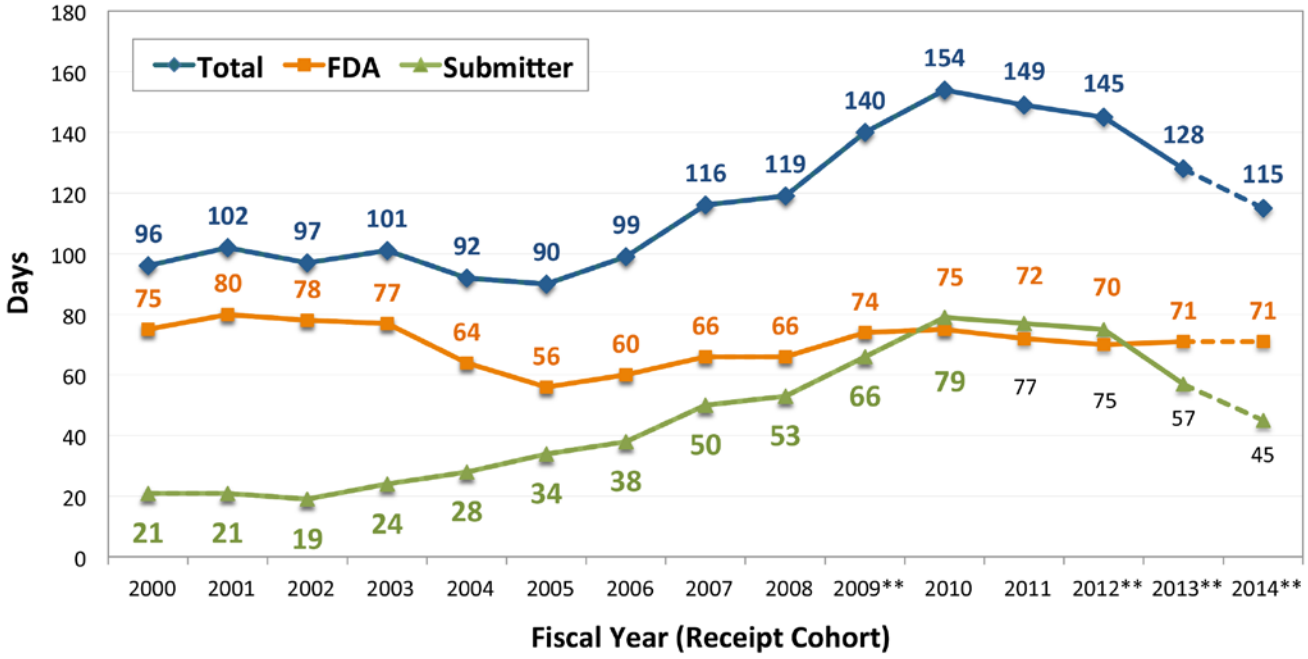

Chart 1. Average time to decision for 510(k) receipt cohorts as of March 31, 2015. Includes SE and NSE decisions only; times may not add to total due to rounding.

***Cohorts still open; percentage of cohort closed: FY 2009 = 99.9%; FY 2012 = 99.9; FY 2013 = 99.9%; and FY 2014 = 88.3% average times for FY 2014 will increase.*

[26] Use of closure level provides a means for fair "apples to apples" comparisons, as performance is compared using the same percentage of work completed in a given year.

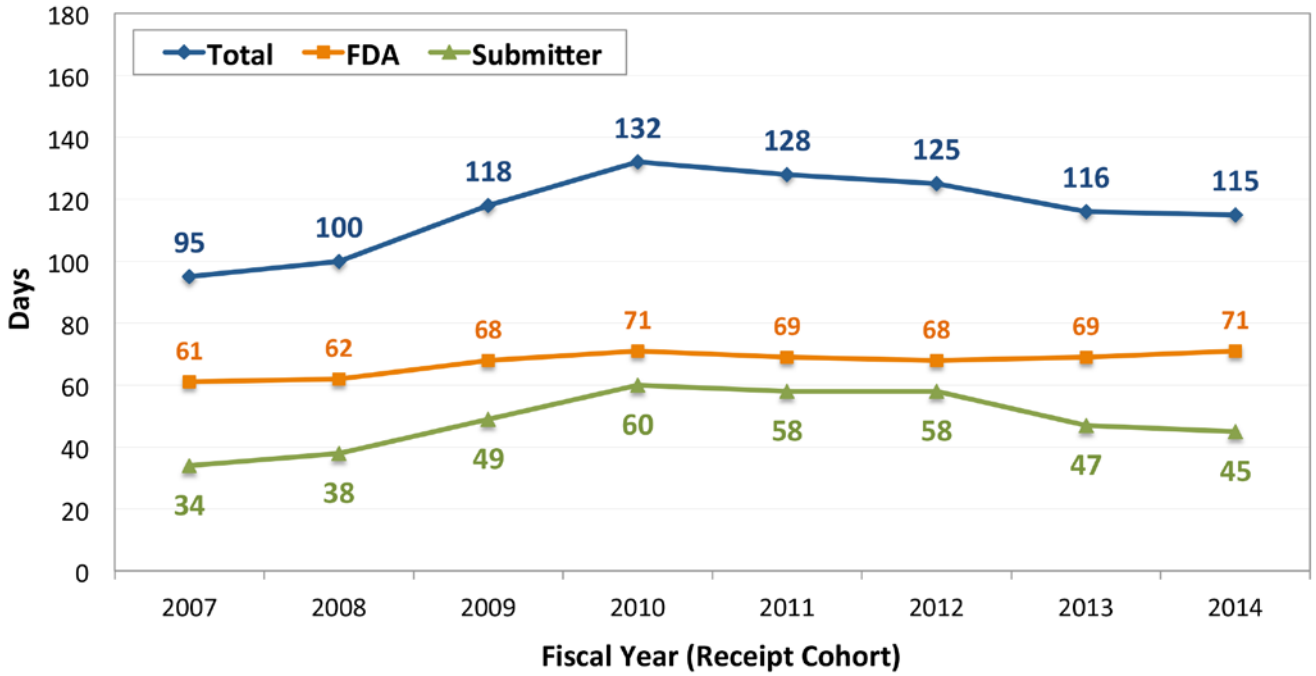

Chart 2. Average time to decision for 510(k). Comparison of receipt cohorts when 88.3 percent closed. SE and NSE decisions only; times may not add to total due to rounding.

Organizationally, the medical device premarket review offices at FDA's Center for Devices and Radiological Health (CDRH) are divided into review divisions, which are composed of review branches. FDA is closing the gap between the branches with the fastest and slowest review times. In 2003, the lowest performing branch reached 34 percent of its 510(k) MDUFA decisions within 90 FDA Days. In 2014, most branches were reaching decisions within 90 FDA Days 90 percent of the time or better, with the lowest performing branch reaching 81 percent of its 510(k) MDUFA decisions within 90 FDA Days.

Substantially Equivalent (SE) Determinations and Pending Submissions: Improvements to the 510(k) program have increased the number of submissions determined to be substantially equivalent (SE) since FY 2011 (decision cohort). The number of submissions determined to be SE in FY 2014 is 11 percent greater than in FY 2010 (**Chart 3**). The effect of CDRH improvements is further observed in the number of pending 510(k) submissions, which has been reduced by 30 percent from its highest level in FY 2010 (**Chart 4**).

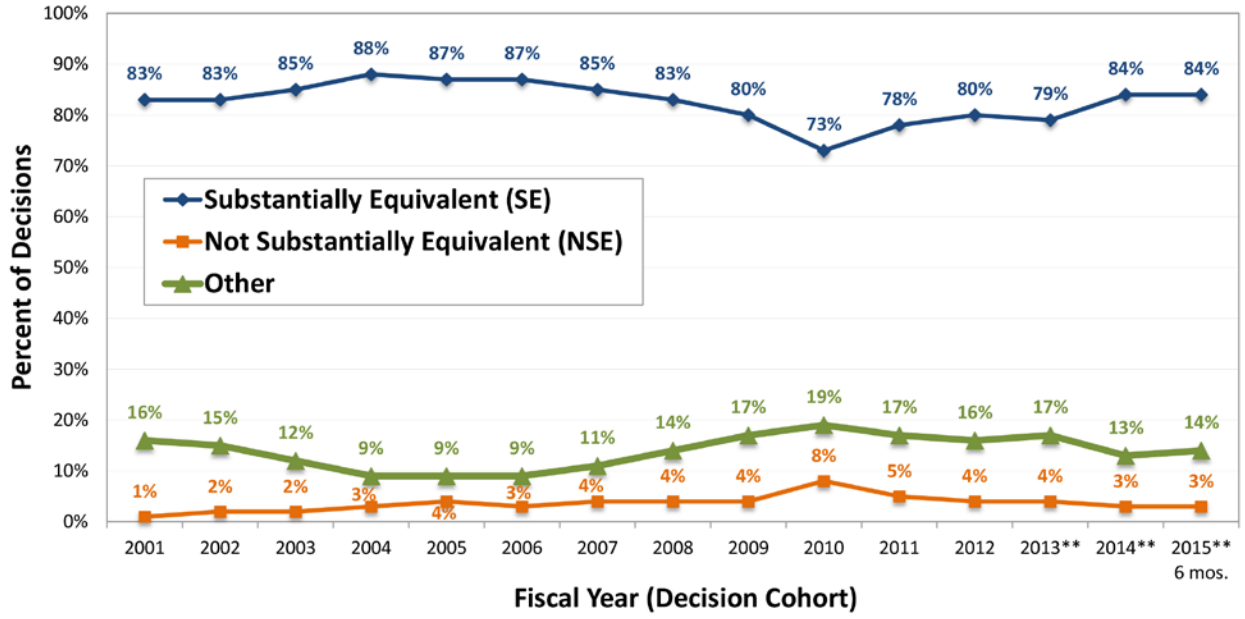

Chart 3. Percent of 510(k) determined to be Substantially Equivalent (SE). Percentages may not add to 100 percent due rounding. FY 2015 includes only 6 months of data.

***Excludes final decisions made on FY 2013 to FY 2015 receipt cohorts that were not accepted for review as of March 31,*

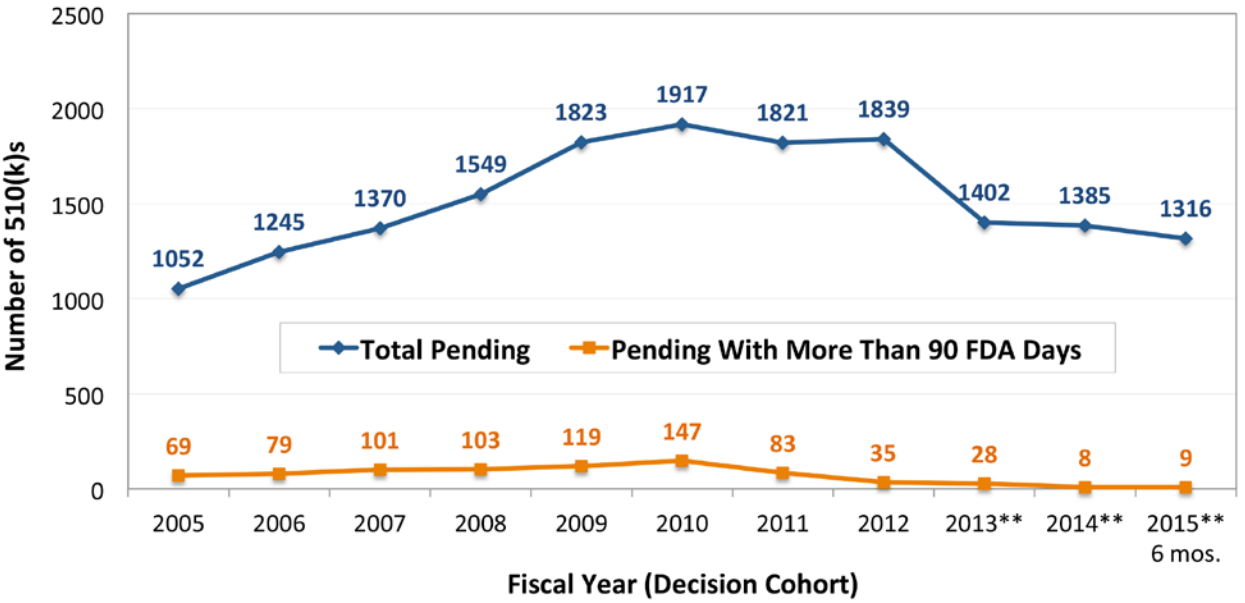

Chart 4. 510(k) submissions pending at end of the fiscal year. Includes 510(k) submissions under review or on hold. FY 2015 is as of March 31, 2015.

***Excludes FY 2013 to FY 2015 receipts that were not accepted for review as of end of year.*

Refuse to Accept (RTA) Policy for 510(k)s: Under RTA, FDA conducts an early review against specific acceptance criteria to assess whether the submission meets a minimum threshold of acceptability and should be accepted for substantive review. The assessment of the completeness of the 510(k) occurs during the early acceptance review, while the assessment of the quality of the submitted information occurs during the substantive review. Since the initiation of the RTA on January 1, 2013, the RTA rate has been decreasing from 58 percent during the second quarter of FY 2013 to 37 percent during the second quarter of FY 2015 **(Chart 5).**

Training and increased FDA and industry experience regarding the RTA process have contributed to the decreased rate while improving the quality of 510(k) submissions. FDA is undertaking a process improvement exercise to further reduce the RTA rate and improve consistency of this program. Overall acceptance rate, when RTA first and second cycles are combined, was 84 percent in FY 2013 and 90 percent in FY 2014.

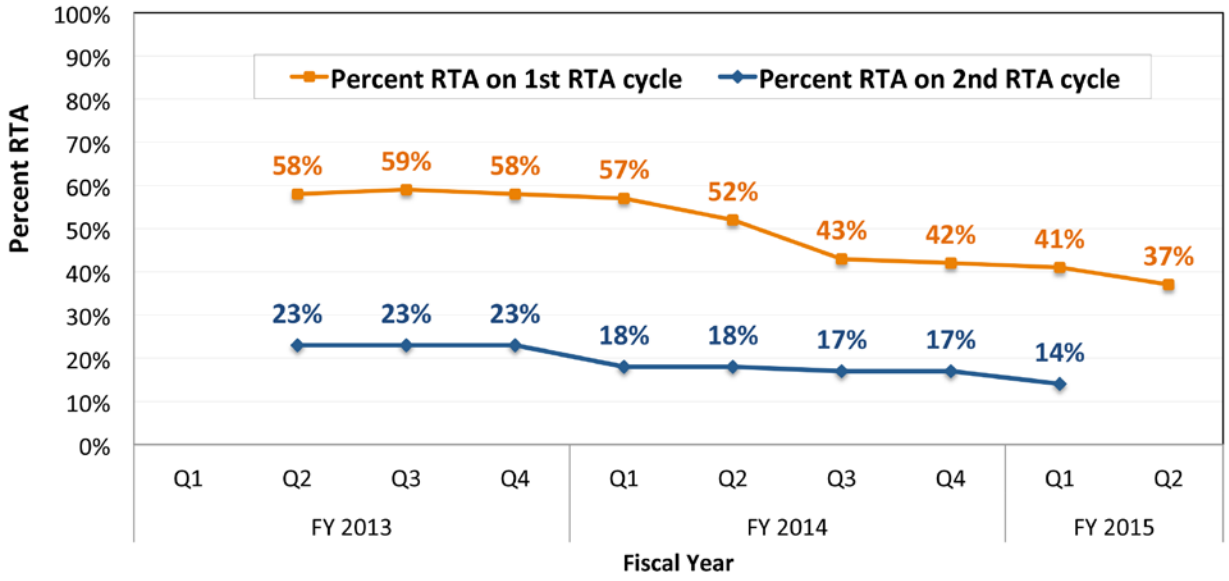

Chart 5. 510(k) Refuse to Accept (RTA) rate for first and second RTA cycles.

Premarket Approval Application (PMA) Program

Average Time to Decision for PMAs: Average time to decision has decreased since its highest point in FY 2009 (**Chart 6**). As of March 31, 2015, the FY 2013 cohort was 83 percent closed and the FY 2014 cohort was 64 percent closed. Comparison of receipt cohorts at the same closure levels show a 36 percent decrease in total review times (**Chart 6**) between FY 2009 and FY 2012, 5 percent decrease in total review times between FY 2009 and FY 2013 (**Chart 7**) when the cohort is 83 percent closed, and a 31 percent decrease in total review times between FY 2009 and FY 2014 (**Chart 8**) when the cohort is 64 percent closed. Once all FY 2014 applications are closed, FDA projects performance will meet or exceed FY 2012 levels, which would be at least a 36 percent improvement since 2009.

Examination of the applications included in these cohorts detected a correlation between average total time to decision and panel meetings (see additional explanation that follows).

FDA is also closing the gap between the divisions with the fastest and slowest review times. Performance has decreased significantly, from a difference in total average days to final decision between the highest and lowest performing divisions of 633 days in FY 2008 to 197 days in FY 2014.

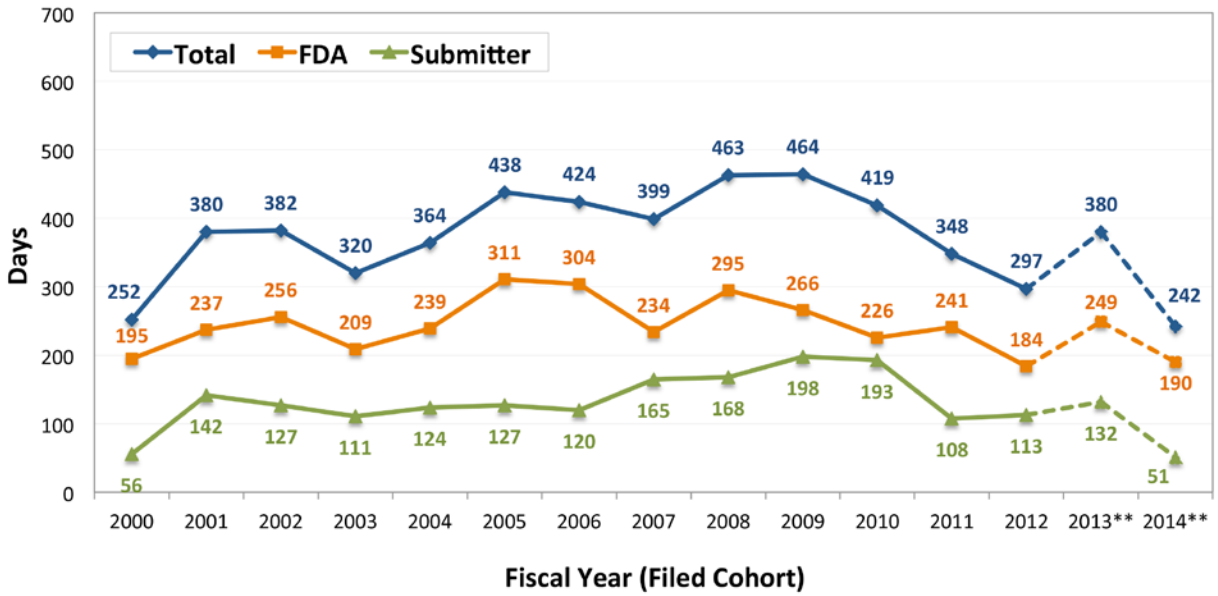

Chart 6. Average time to MDUFA decision for PMAs, as of March 31, 2015. Includes original PMAs only; FY 2013 to FY 2014 are receipt cohorts including PMAs filed as of March 31, 2015. Prior cohorts are filed cohorts; times may not add to total due to rounding.

***Cohorts are still open, average times will increase percentage of cohort closed: FY 2013 = 83% (24/29); FY 2014 = 64% (18/28).*

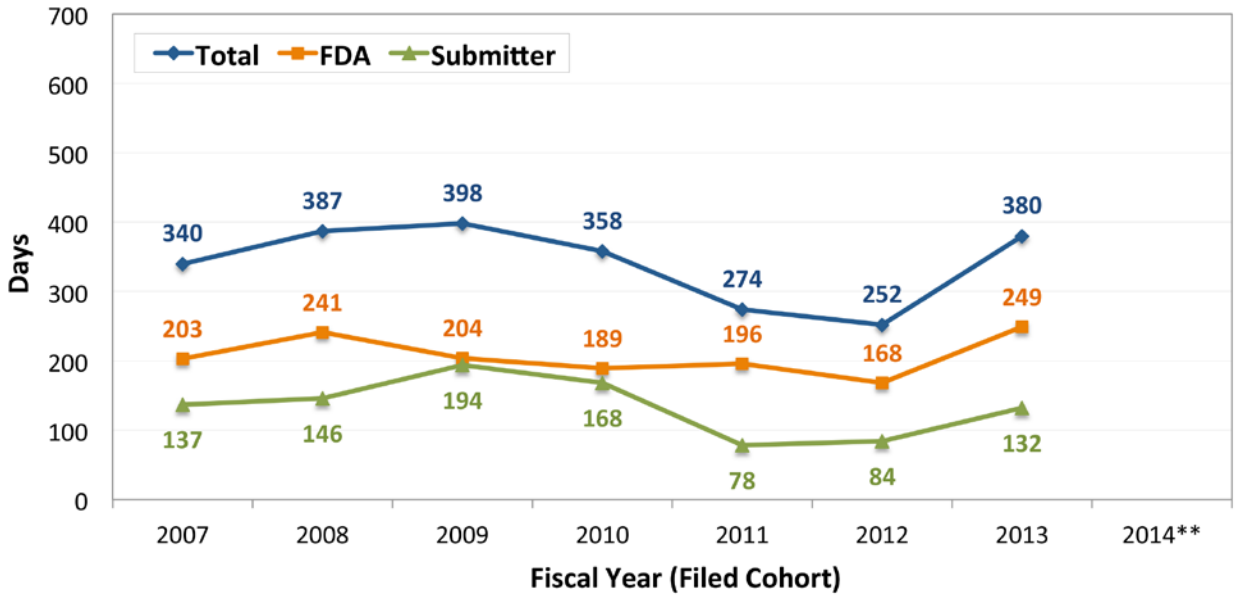

Chart 7. Average time to MDUFA decision for PMAs. Comparison of filed cohorts when approximately 83 percent closed. Includes original PMAs only; times may not add to total due to rounding.

*** FY 2014 cohort is not yet 83% closed (as of March 31, 2015).*

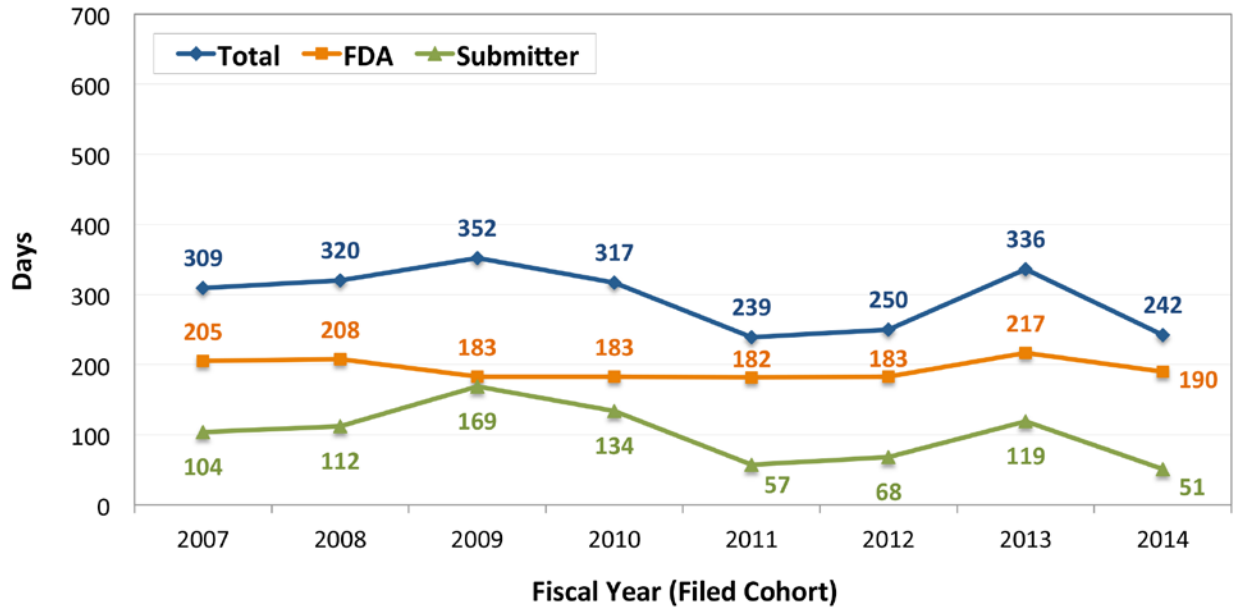

Chart 8. Average time to MDUFA decision for PMAs. Comparison of filed cohorts when approximately 64 percent closed. Includes original PMAs only; times may not add to total due to rounding.

Effect of an Advisory Panel Meeting on Average Total time to Decision: As part of the review process, FDA may present a PMA to an expert advisory panel for its recommendations. Medical device advisory committees provide independent, professional expertise and technical assistance on the development, safety and effectiveness, and regulation of medical devices. PMAs that undergo an advisory panel review have different performance goals than PMAs that do not go to an advisory panel because holding an advisory panel meeting adds more time to a review. Examination of the FY 2013 cohort shows the highest percentage of PMAs undergoing an advisory panel review since 2007, which led to what appears to be an increase in review times. But when "apples-to-apples" comparisons are made, total review times continue to show a decrease.

PMAs that undergo an advisory panel review typically take longer to reach a final decision, as accounted for in MDUFA III performance goals. Because the average total time includes both PMAs that go and do not go to an advisory panel meeting, the spike in review time for FY 2013 reflects the significantly higher percentage, 38 percent (**Chart 9**), of applications with an advisory panel meeting. However, when comparing review times of PMAs with a panel meeting (**Chart 10**) across different years and PMAs without panel meetings across different years, we continued to see improved performance in FY 2013 for both categories of PMAs. In addition, the percent of PMAs that will undergo advisory panel review in FY 2014 is considerably less than FY 2013. A decrease in the percent of PMAs which will go to an advisory panel meeting in FY 2014 along with other program improvements lead FDA to expect lower average total review times in FY 2014.

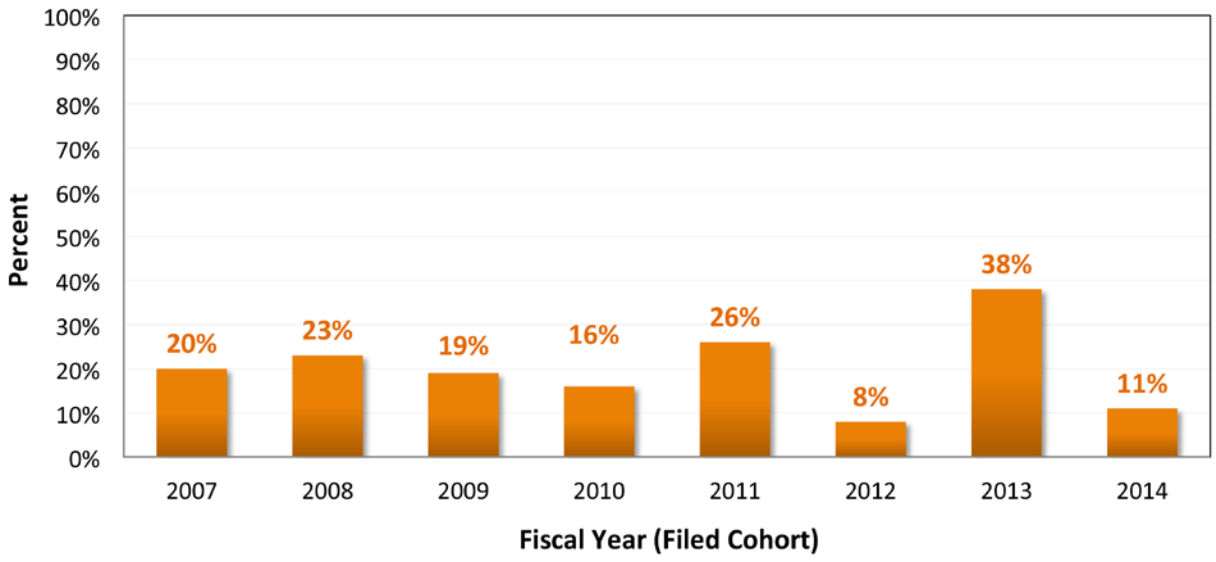

Chart 9. Percentage of PMAs with panel review, as of March 31, 2015, based on PMAs with a MDUFA decision.

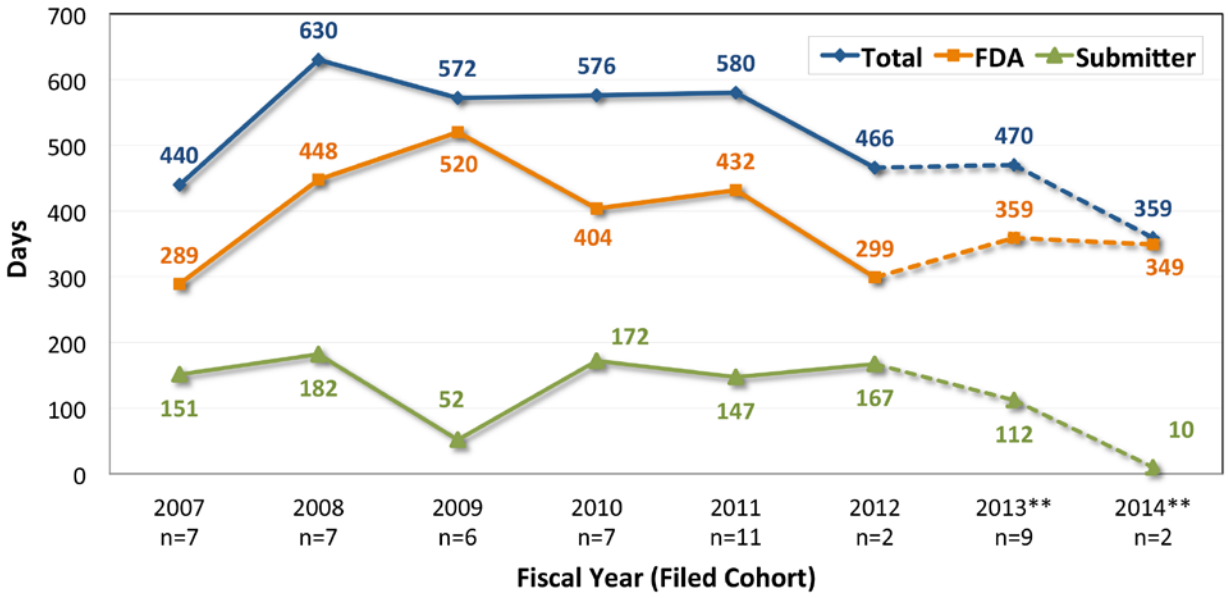

Chart 10. Average time to MDUFA decision for PMAs with panel review, as of March 31, 2015. Includes original PMAs only; FY 2013 to FY 2014 are receipt cohorts including PMAs filed as of March 31, 2015. PMAs for prior cohorts are filed cohorts; times may not add to total due to rounding.

***Cohorts are still open, average times will increase; percentage of cohort with MDUFA decision: FY 2013 = 90% (9/10); FY 2014 = 67% (2/3)*

Approved and Pending PMAs: Improvements to the PMA program have resulted in an increase in the number of applications approved since 2011 (decision cohort). The number of applications approved in FY 2014 was 31 percent greater than FY 2010 (**Chart 11**). The impact of CDRH improvements is further observed in the number of pending original PMAs, which has been reduced by 46 percent from its highest level in FY 2010 (**Chart 12**). Note that the FY 2015 cohort only includes six months of data.

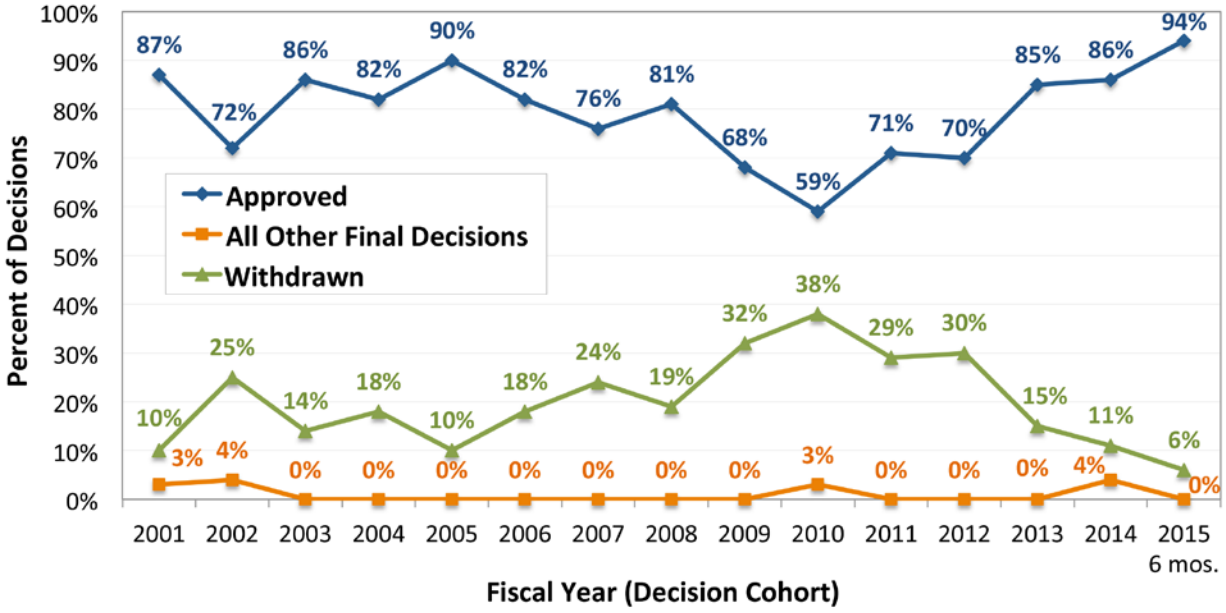

Chart 11. Percentage of PMAs approved. Based on original PMAs that were accepted for filing as of March 15, 2015; percentages may not add to 100 percent due to rounding.

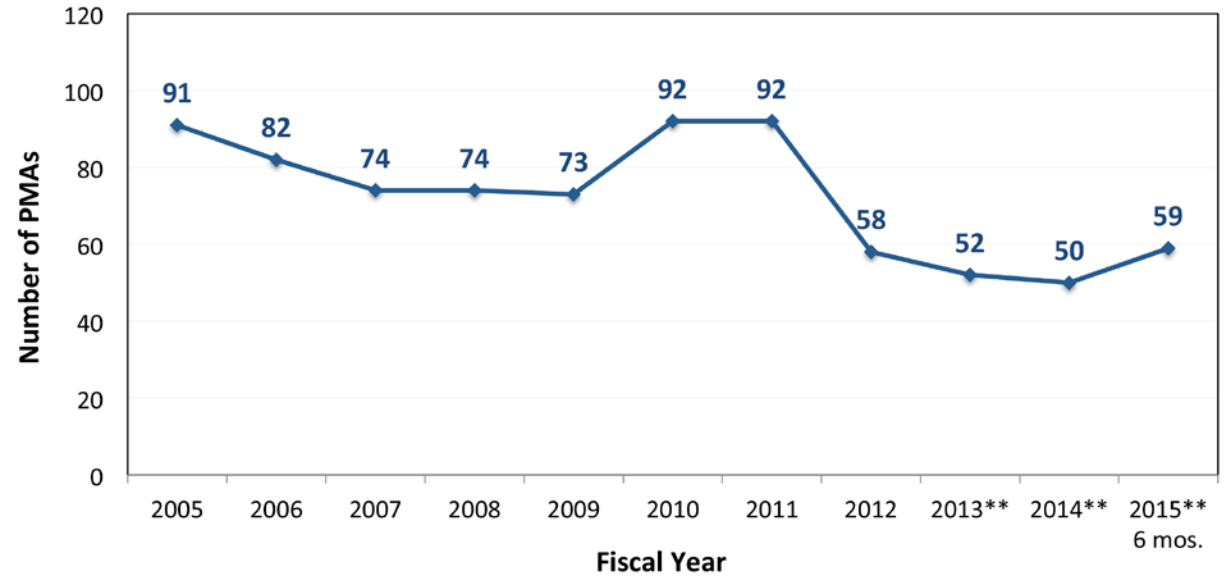

Chart 12. PMAs pending at the end of the fiscal year. Includes original PMAs under review or on hold. FY 2015 is as of March, 31, 2015**.**

***Excludes FY 2013 to FY 2015 receipts not accepted for review at year's end.*

De Novo Program

Average Time to *De Novo* Granting: Improvements to the de novo program have resulted in a 70 percent reduction in the average total time to decision for these submissions. Average total time to final *de novo* decision for devices with post-NSE de novo requests (includes FDA and Submitter Days for 510(k) NSE review and post-NSE de novo review) has been reduced from 992 days in FY 2010 to 300 days in FY 2014. Average total time to decision for direct *de novo* requests are even lower than for *de novo* requests using the post-NSE review pathway (**Chart 13**). While time to decision has significantly decreased since FY 2010, the number of *de novo* requests received has almost doubled (25 *de novo* requests in FY 2010 versus 46 and 41 in FY 2013 and FY 2014, respectively).

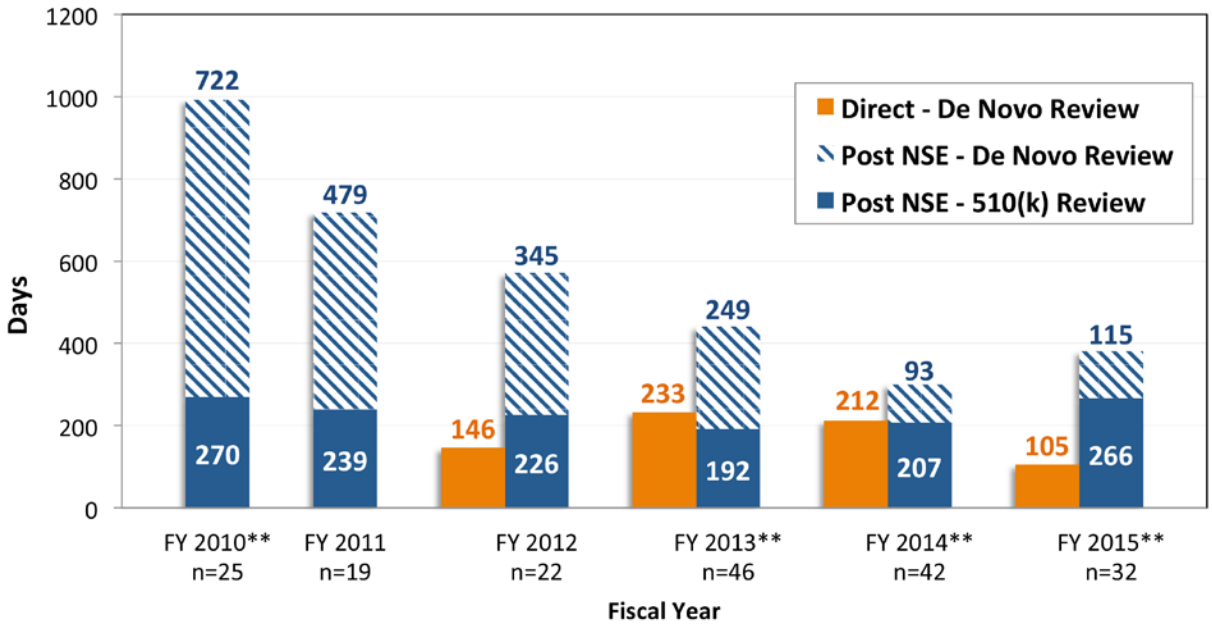

Chart 13. **Average total time to final *de novo*** decision for devices with post-NSE *de novo* request and devices with direct *de novo* requests. Data as of March 31, 2015.

***Cohort still open.*

Investigational Device Exemption Program

IDEs Approved within Two Cycles: Improvements to the IDE Program (e.g., establishing a formal Clinical Trials Program, process improvements, policy changes, extensive training for CDRH review staff and the device industry, and new guidance documents) have greatly shortened the time for an IDE to reach approval, so that a clinical trial can begin. The number of IDE studies that are fully approved within two cycles has increased significantly. The FY 2014 percentage of fully approved IDE studies within one cycle increased nine-fold compared to FY 2011. And the percentage fully approved within two cycles increased four-fold compared to FY 2011. In FY 2014, 63 percent of IDEs submitted were approved within 2 cycles. Current FY 2015 percentages show even greater improvements (**Chart 14**).

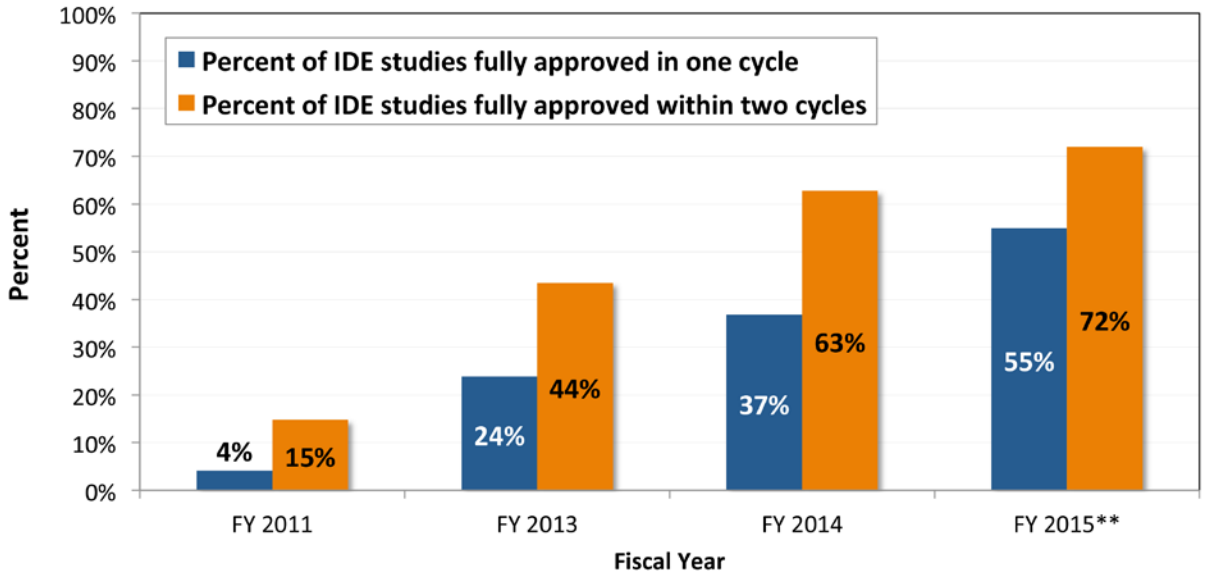

Chart 14. Percentage of IDE studies fully approved within one and two cycles.

***FY 2015 cohort still open.*

Median Number of Days to IDE Full Approval: The median number of days to full IDE approval has decreased from 442 in FY 2011 to only 101 in FY 2014, reducing the time it takes to bring a new medical device to market by nearly a full year. As of March 31, 2015, the FY 2015 median number of days is 30 days (**Chart 15**).

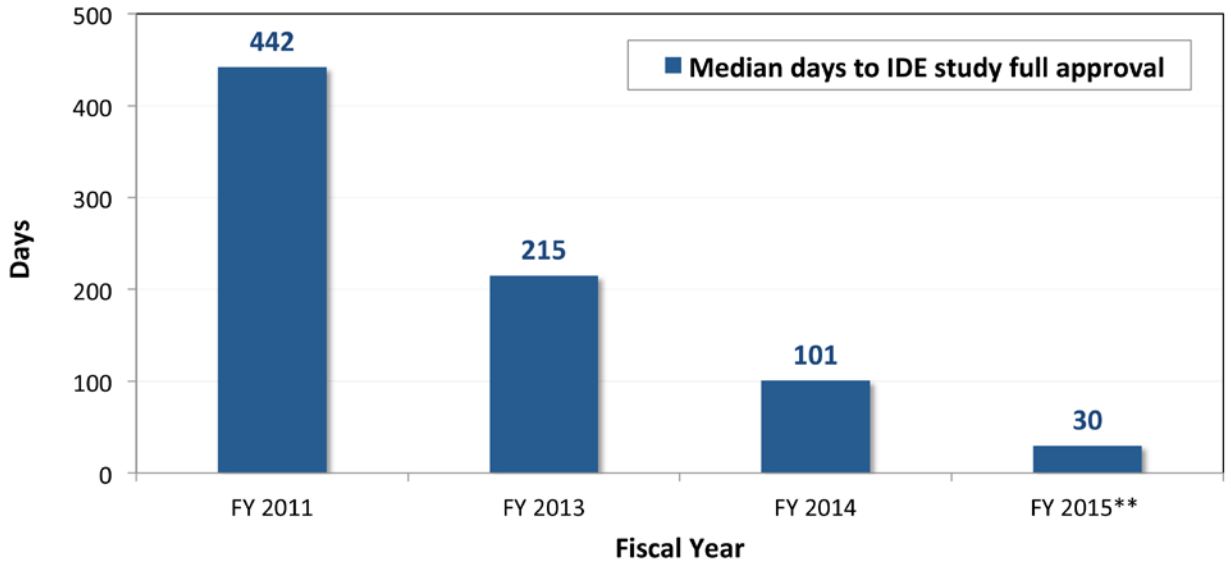

Chart 15. Median number of days to full IDE approval.

***FY 2015 cohort still open.*

Clinical Studies: Devices that are studied in the United States in the early stages of development are more likely to reach American patients sooner in pivotal studies and as marketed devices. In the past 15 fiscal years, for those original PMAs whose approval was based on FDA-approved pivotal clinical studies, 94 percent (283 out of 300) of these approvals were based on a single pivotal clinical study. More recently, in the past five years, the number has increased to 98 percent (82 out of 84). Of the 82 FDA approved original PMAs whose approval was supported by a single pivotal clinical study, 32 (39 percent) included studies enrolling subjects outside the United States. For *in vitro* diagnostic devices (IVD), where clinical studies are typically conducted in at least three sites, sponsors generally choose to have one of those sites inside the United States to address differences between the United States and other countries in how medicine is practiced, patient populations, and disease progression.

FDA is facilitating and encouraging the use of innovative clinical trial designs and statistical methods such as adaptive clinical trials and Bayesian statistics. For the period from 2007 to May of 2013, FDA received 250 submissions that were adaptive, most of which were pre-submissions and IDEs. About 30 percent of these used Bayesian methodologies. In addition, there were 17 PMAs and PMA Supplements that used adaptive clinical trials from 2007 to May of 2013, eight of which used Bayesian methodologies.

Customer Satisfaction

Customer Service Rating: Excellent customer service means understanding and addressing, as appropriate, stakeholders' and colleagues' needs through active listening, problem solving, seeking out ideas, explaining the rationale for FDA decisions and requests for information, learning from mistakes, and doing FDA's best work. Providing excellent customer service improves agency interactions and supports better regulatory outcomes, thereby improving patient health.

By providing excellent customer service, FDA does not alter the agency's regulatory obligations. Customer service does not mean letting unsafe or ineffective devices on the market; rather, it involves identifying and meeting customers' needs, as appropriate, while achieving the agency's mission and vision.

The experience of receiving excellent customer service can encourage device makers to choose the United States first when bringing their products to market; in turn, U.S. healthcare providers gain access to the technologies that they need to administer quality health care to patients. In June 2014, FDA's Center for Devices and Radiological Health (CDRH) began measuring customer satisfaction and established a goal of 70 percent satisfaction by the end of 2014. The center's performance was 83 percent (95 percent confidence level and 2 percent margin of error). The performance of the premarket program was 86 percent satisfaction (95 percent confidence level and 3 percent margin of error). Among its industry stakeholders—industry, industry consultants, and industry trade associations—satisfaction was even higher at 89 percent (95 percent confidence level and 4 percent margin of error).

As of March 31, 2015, this FDA center was exceeding its June 2015 goal of 80 percent customer satisfaction, with an 88 percent customer satisfaction rating. As of the same date, satisfaction with the premarket program was 93 percent (**Chart 16**), and the premarket "industry" satisfaction rating was 96 percent.

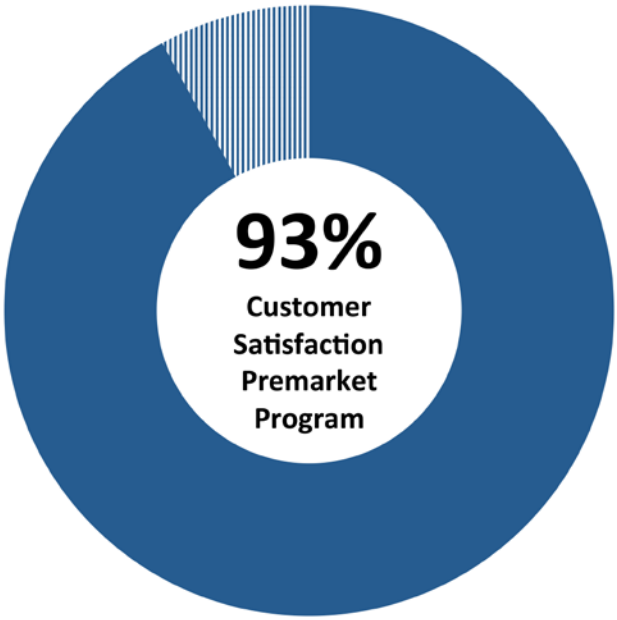

Chart 16. Premarket program 2015 customer satisfaction rating. As of March 31, 2015. The satisfaction score includes respondents who indicated they have interacted with CDRH's premarket offices.